# Engineered biomaterials for combination cancer immunotherapy

James J. Moon[1,2,3,*]

[1] *Department of Pharmaceutical Sciences, University of Michigan, Ann Arbor, MI 48109, USA.*
[2] *Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI 48109, USA.*
[3] *Biointerfaces Institute, University of Michigan, Ann Arbor, MI 48109, USA.*
*E-mail address: moonjj@med.umich.edu*

With profound advances in immune-oncology, cancer immunotherapy is now considered the fourth pillar of cancer therapy, joining the ranks of surgery, radiotherapy, and chemotherapy. However, only a small subset of cancer patients responds to cancer immunotherapy. While the combination of multiple immune checkpoint blockers generally improves the clinical responses, this can lead to severe immune-related adverse events that result in clinical manifestations of dermatitis, colitis and hepatitis. Thus, new approaches are needed to amplify anti-tumour T-cell immune responses, to convert cold tumours into hot tumours, and to sensitize tumours to immunotherapies with minimal immune-related adverse events. Here, we present new biomaterial-based strategies for amplifying anti-tumor immune responses and sensitizing tumors to immunotherapies in a safe and effective manner. Briefly, we show that lipid-based nanodiscs can efficiently co-deliver antigen and immunostimulatory molecules to draining lymph nodes and elicit potent CD8+ cytotoxic T lymphocyte responses directed against tumor antigens, leading to substantially enhanced anti-tumor efficacy in multiple murine tumor models, including colon carcinoma, melanoma, and glioblastoma multiforme. We have also demonstrated their efficacy in non-human primates. In a second research thrust, we are developing new biomaterials for *in situ* modulation of the gut microbiome for regulation of local and systemic immune responses. We will share our latest results showing the therapeutic potential of our gut modulation approach in the context of improving the safety and efficacy of immune checkpoint blockers. Owning to the facile manufacturing process, robust therapeutic efficacy, and good safety profiles, our biomaterial-based approaches may offer powerful and convenient platforms for improving cancer immunotherapy and cancer patient outcomes.

*Key Words:* nanomedicine, gut microbiome, cancer immunotherapy, vaccine

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